plurality of the predicted mass spectrum patterns,

$$S(i) = I(i) - \sum_{n=1}^{m} w(n) I(i-n)$$

wherein m represents a predetermined natural number and w(n) represents a factor for the measured mass spectrum of the sample measured at n-th before the measurement of the sample which is measured at i-th.

REMARKS

The Examiner, Mr. Chakrabarti, is thanked for the courtesy extended applicants' attorney during the interview of June 5, 2003, during which time differences between the claimed invention and the cited art were discussed as well as amendments considered to overcome the rejection of the claims under 35 U.S.C. §112, first and second paragraphs. As indicated in the Interview Summary, the Examiner advised applicant to amend the independent claim 1, for example, to make it a method claim which amendment may overcome the 102 rejection, and that by submission of such amendment, favorable consideration would be given, although search would be necessary. Applicants note that by the present amendment, the claims have been amended in a manner which is considered to overcome the rejection under 35 U.S.C. §112, first and second paragraphs, with the specification also being amended to correct minor informalities and to clarify features of the present invention.

Turning to the Examiner's suggestion to convert the apparatus claims 1-15 into method claims, claims 1-15 have been amended in the manner suggested by the Examiner, noting that claims 16-20 present in this application are method claims, which have been considered by the Examiner. Applicants submit that by the present amendment, all claims are now method claims, and such claims have been amended in a manner which is considered to be in compliance with 35 U.S.C. §112, first and second paragraphs, and patentably distinguish over the cited art, as will become clear from the following discussion.

As to the rejection of claims 1-20 under 35 U.S.C. §112, second paragraph, this rejection is traversed insofar as it is applicable to the present claims, and reconsideration and withdrawal of the rejection are respectfully requested.

In setting forth the rejection, the Examiner indicates that with regard to claim 1, the phrase "including" renders the claim indefinite, and that claims 4 and 13-20 are indefinite over the recitation of the phrase "level of influence". By the present amendment, as discussed with the Examiner at the interview, the recitation in claims 1, 13-15, which previously utilized the terminology of "both an information including a" has been amended to recite "both an information about the number...and an information..." which the Examiner has indicated overcomes the previous indefiniteness. Likewise, the recitation in claims 4, 13-15 and 19 concerning w(n) represents a factor "that represents a level of influence of the sample measured..." has been amended to recite the feature that w(n) represents "a factor for the measured spectrum of the sample measured..." as clearly described in the specification of this application, such that as indicated by the Examiner at the interview, the indefiniteness noted should be overcome. Accordingly, applicants submit that all claims present in this application should now be considered to be in compliance with 35 U.S.C. §112, second paragraph.

With respect to the rejection of claims 4 and 13-20 under 35 U.S.C. §112, first paragraph, this rejection is traversed insofar as it is applicable to the present claims, and reconsideration and withdrawal of the rejection are respectfully requested.

Applicants note that in setting forth the rejection, the Examiner contends that the specification, while being enabling for weighting factors as disclosed at page 21 of the specification, does not reasonably provide enablement for any number w(n). Contrary to the position set forth by the Examiner, applicants note that by the present amendment of the specification, reference is made to "time" rather than "hours" and as described in the paragraph bridging pages 20 and 21 of the specification, w(1) is determined from the ion intensity measured at the time after T

from the time at which the maximum ion intensity is measured and also the ion intensity measured at the time after 2T is determined from w(2). As is apparent to those of ordinary skill in the art from the description, w(3) is determined by measurement of the ion intensity measured at the time after 3T while w(4) is determined after 4T, etc. Thus, applicants submit that the specification and the claims should be considered to be in compliance with 35 U.S.C. §112, first paragraph.

Applicants submit that it is apparent that since the term "w(n)" does not appear in independent claims 1 and 16, and claims 5, 6, 17, 18 and 20 do not depend directly or indirectly from a claim utilizing "w(n)", such claims are not subject to the rejection under 35 U.S.C. §112, first paragraph. It is noted, however, that for example, with respect to claim 1, which applicants submit patentably distinguish over the cited art as will be discussed below and dependent claim 4, independent claims 13-15 recite the features of claim 1 therein in addition to other features, and applicants submit that all claims should now be considered to be in compliance with 35 U.S.C. §112, first paragraph. Thus, applicants submit that this rejection should be overcome.

As to the rejection of claims 1-3 and 5-6 under 35 U.S.C. 102(b) as being anticipated by Koster (U.S. Patent 5,605,798); the rejection of claims 7-10 under 35 U.S.C. 103(a) over Koster (U.S. Patent 5,605,798) in view of Haff et al (U.S. Patent 5,885,775); and the rejection of claims 11 and 12 under 35 U.S.C. 103(a) over Koster (U.S. Patent 5,605,798) in view of Haff et al (U.S. Patent 5,885,775) and further in view of Harris et al (U.S. Patent 4,353,242); such rejections are traversed insofar as they are applicable to the present claims, and reconsideration and withdrawal of the rejections are respectfully requested.

B At the outset, as to the requirements to support a rejection under 35 U.S.C. 102, reference is made to the decision of In re Robertson, 49 USPQ 2d 1949 (Fed. Cir. 1999), wherein the court pointed out that anticipation under 35 U.S.C. §102

requires that each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. As noted by the court, if the prior art reference does not expressly set forth a particular element of the claim, that reference still may anticipate if the element is "inherent" in its disclosure. To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." Moreover, the court pointed out that inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

With regard to the requirements to support a rejection under 35 U.S.C. 103, reference is made to the decision of In re Fine, 5 USPQ 2d 1596 (Fed. Cir. 1988), wherein the court pointed out that the PTO has the burden under §103 to establish a prima facie case of obviousness and can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. As noted by the court, whether a particular combination might be "obvious to try" is not a legitimate test of patentability and obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. As further noted by the court, one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

Furthermore, such requirements have been clarified in the recent decision of In re Lee, 61 USPQ 2d 1430 (Fed. Cir. 2002) wherein the court in reversing an obviousness rejection indicated that deficiencies of the cited references cannot be remedied with conclusions about what is "basic knowledge" or "common knowledge". The court pointed out:

The Examiner's conclusory statements that "the

> demonstration mode is just a programmable feature which can be used in many different device[s] for providing automatic introduction by adding the proper programming software" and that "another motivation would be that the automatic demonstration mode is user friendly and it functions as a tutorial" do not adequately address the issue of motivation to combine. This factual question of motivation is immaterial to patentability, and could not be resolved on subjected belief and unknown authority. It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to "[use] that which the inventor taught against its teacher."... Thus, the Board must not only assure that the requisite findings are made, based on evidence of record, but must also explain the reasoning by which the findings are deemed to support the agency's conclusion. (emphasis added)

Irrespective of the Examiner's position concerning the disclosure of Koster, as recognized by the Examiner, Koster does not disclose the method as recited in the claims of this application. More particularly, applicants submit that there is no disclosure in Koster of predicting mass spectrum patterns in at least two cases based upon the test DNA fragment and as recited in claim 1, for example, and "comparing a plurality of the predicted mass spectrum patterns with the measured mass spectrum to determine nucleic acid base on the polymorphism point" (emphasis added). Applicants note that Koster discloses detection of a wild type and/or mutant sequence in a target nucleic acid molecule referring to Fig. 1c, col. 11, line 57 to col. 12, line 16 and col. 5, lines 9-14, wherein a mutant is distinguished from a wild type by mass spectrometry. That is, a mutant and a wild type are distinguished based on a comparison of measured mass spectra, such that there is no disclosure or teaching in Koster of the comparison of a plurality of predicted mass spectrum patterns with the measured mass spectrum to determine a nucleic acid based on the polymorphism point. As is apparent, there is no disclosure or teaching in the sense of 35 U.S.C. 102 or 35 U.S.C. 103 regarding the comparing step as recited in each of the independent claims of this application, such that applicants submit that all claims patentably distinguish over Koster in the sense of 35 U.S.C.

102 and 35 U.S.C. 103, and all claims should be considered allowable thereover.

Additionally, irrespective of whether or not Koster discloses ionization and mass spectrometry, applicants submit that Koster does not generate plural kinds of multiply-charged ions of a test DNA fragment by ionization, where each of the multiply-charged ions has five or more charges, which feature is recited in each of the independent claims of this application. Although Koster mentions a generation of multiple ion peaks (col. 11, lines 6-8), Koster does not disclose the generation of multiply-charged ions and although Fig. 11 and Example 2 provides a description of the mass spectrum, Koster does not describe the valance of ions and ions having five or more charges. Further, it is readily apparent that there is no disclosure or teaching in Koster of performing the treatment utilizing the formula for the measured mass spectrum as recited in claims 4, 13-15 and 19. Thus, applicants submit that these features as recited in the independent and dependent claims of this application are not disclosed or taught by Koster and all claims patentably distinguish thereover.

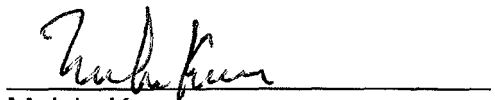
With respect to the addition of Haff et al and Harris et al, applicants note that such references are not utilized to overcome the deficiencies of Koster other than for emergency information and the use of plural measurement systems. However, these references do not overcome the deficiencies of Koster as pointed out above, and applicants submit that the proposed combination fails to provide the claimed features in the sense of 35 U.S.C. 103. Thus, applicants submit that all claims present in this application should now be in condition for allowance.

As is apparent from the above, claims of this application were not properly rejected under 35 U.S.C. §112, first and second paragraphs, and were not rejected over the cited art, such that these claims, such as claims 16-18 and 20 directed to the method should stand allowed. By the present amendment, the rejection of the appropriate claims under 35 U.S.C. §112, first and second paragraphs, have been overcome, and all claims have been presented in a method format and as

recognized by the Examiner at the interview, all claims should now receive favorable consideration. Accordingly, issuance of an action of a favorable nature is courteously solicited.

To the extent necessary, applicant's petition for an extension of time under 37 CFR 1.136. Please charge any shortage in the fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account No. 01-2135 (1021.40593X00) and please credit any excess fees to such deposit account.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Page 14, please amend the paragraph beginning at line 14 as follows:

A liquid sample contains various kinds of DNA fragments prepared by the sample treatment part 11. The liquid sample is kept in a sample-retaining vessel such as a 384-hole microtiter plate. On the other hand, a cleaning fluid is stored in the container 12 and is then passed into the sampling part 15 through a capillary tube 13 at a predetermined flow rate. In the sampling part 15, the sample-retaining vessel is transferred from the sample treatment part 11 into position. A sampling operation is then initiated by a control signal from the control unit 31. The sample may be introduced from the sampling part 15 into the ionization part 21 by passing the sample along the capillary tube ~~13~~ 16 at a predetermined ~~frequency~~ time period of, for example once per five seconds. Therefore, the sample can be introduced into the ionization part 21 at a predetermined ~~frequency~~ time period T, while the cleaning fluid is introduced into the ionization part 21 during the remainder of the time period. Typically, the sample may be introduced into the ionization part 21 for one second and subsequently the cleaning fluid is introduced for 4 seconds. These steps may be repeated in cycles.

Page 17, please amend the paragraph beginning at line 3 as follows:

Each sample to be prepared in the sample treatment part 11 has its own individual label number. The sample treatment part 11 links such a label number with the information about a predicted SNP portion, followed by sending to the output prediction part 32. In the output prediction part 32, a predicted pattern of a mass spectrum (i.e., a prediction of the relative intensity distribution of the mass spectrum) is calculated. The results of such a calculation are transmitted to the data analysis part 33. The control part 31 sends out a sampling start signal to the sampling part

15. Simultaneously, the control part 31 sends out the label number to the output analysis part 35 so as to link an output of the detector 28 in the mass spectrometric part 24 with the label number of the sample. The output subjected to the output analysis in the output analysis part 35 is transmitted to the data analysis part 33. Among the predicted mass spectrum patterns sent from the output prediction part ~~35~~ 32, a prediction having the highest level of matching score (homology) is defined. Then, the results are sent to the recording part 34 and stored together with the label number on a recording medium.

Page 19, please amend the paragraph beginning at line 19 as follows:

In the equation, S(i) denotes the result of the output-analysis of the sample introduced at ~~ith~~ i-th, obtained from the output analysis part 35; I(i) denotes an output from the detector 28 of the mass spectrometric part 24 to the output analysis part 35 with respect to a sample introduced at ~~ith~~ i-th in the order of samples to be measured; w(n) denotes an attribute that represents a degree of the influence (interference) of a sample introduced at (i - n)th in the order of the samples against a measurement value of the sample introduced at ith, which is obtained by actual measurement. For example, if n = 0, then w(0) =1; and m denotes a predetermined natural number. The above equation means that the influences of the remainder of the measurement sample introduced at (i - m)th in the order of the samples is removed from the output I(i) of the detector 28.

Page 20, please amend the paragraph beginning at line 11 as follows:

A factor w(n) can be defined by measuring that the changes in the ion intensities over time detected by the detector 28. If a sample is once introduced into the flow of a cleaning fluid, then the detector 28 of the mass spectrometric part 24 detects the changes in ion intensities of the sample over time. In this case, the ion intensity steeply rises at first and then gradually decreases over time as the genome DNA sample being absorbed on the inner surface of the capillary tube 16 becomes

removed and dispersed therefrom. The w(n) can be determined by measuring a relative ion intensity after the time "T x n" ~~hours~~ from the time at which the maximum ion intensity is observed. In other words, if the maximum ion intensity is 1 (one), then w(1) is determined from the ion intensity measured at the time after T ~~hours~~ from the time at which the maximum ion intensity is measured and also the ion intensity measured at the time after 2T ~~hours~~ is determined from w(2).

Page 21, please amend the paragraphs beginning at lines 4 and 15 as follows:

In the actual measurement, the samples that contain genome DNA are intermittently infused into the capillary tube 16 at predetermined intervals (T). In this case, however, the cleaning fluid is circulated in the tube 16. If the time T is more than several minutes, the factor w(1) is so small to be almost negligible. If the time T becomes small, for example in the case of T = 4 seconds, then the factor w(1) becomes considerably large. It means that the contamination of the sample arises. Therefore, the processing such as the one indicated by the equation (1) is required.

Fig. 2 shows charts of mass spectra that illustrate an output I(i) from the detector 28 of the mass spectrometric part 24, and outputs S(i), S(i - 1), and S (i - 2) from the output analysis part 35. In this case, the factor w(n) is input in the output analysis part 35 in advance. In the example shown in the figure, the influences of the sample S(i - 1) measured by the immediately preceding measurement and the influences of the sample S(i -2) measured by the measurement preceding the above measurement remarkably appear on the actual output I (i) from the detector 28. Furthermore, the degrees of these influences are more increased when the sample is subjected to the more recent measurement. Therefore, the measurement value S(i) can be obtained only for the ~~ith~~ i-th sample by performing a weighting and subtracting ~~S(i - 1)~~ I(i-1) and ~~S(i - 2)~~ I(i-2) from the output I (1) of the detector 28 of the mass spectrometric part 24. Fig. 3 shows an example of actual data obtained by the genome DNA analysis system of the present invention. Figs. 3A, 3B, and 3C

represent the examples of the output results (mass spectra) when the samples with genome DNA of 20 base length, 30 base length, and 40 base length are measured. The horizontal axis of the graph represents the value of mass-to-charge ratio (m/z) obtained by dividing the mass m of ion with the number z of charges, and the vertical axis thereof represents a relative ion intensity.

Page 25, please amend the paragraph beginning at line 16 as follows:

Fig. 4 indicates a typical example showing an ion intensity distribution (a distribution profile of peaks) of a mass spectrum to be measured. A relative ion intensity corresponding to "z" or "m/z" can be predicted while the distribution of ion intensities (distribution profile of peaks) as shown in Fig. ~~5~~ 4 by a broken line is previously determined. It is possible to perform a data analysis with the predictive information using "m/z" of the detected ion only. The analytic accuracy can be increased as the information of the relative ion intensities is added. It is more effective that the information of the relative ion intensity is considered in addition to the value of m/z when the detected ion peak is extremely weak or genome DNA sample is multiplexed.

Page 33, please amend the paragraph beginning at line 9 as follows:

An analysis system used for the present embodiment may be the system shown in Fig. 1. In this case, however, the sample-treatment part 11 can simultaneously perform the procedures of PCR amplification, extension and the like on the predetermined number (n) of different genome DNA fragments to prepare a sample that contains a mixture of the predetermined number (n) of the different genome DNA fragments with different base lengths. In the sampling part 15, a predetermined volume of the sample which makes up the genome DNA fragments having different base lengths is introduced into the capillary tube 16 at ~~a regular interval~~ predetermined intervals of T. The mass spectrometric part 24 simultaneously performs the measurement on the predetermined number (n) of the

different genome DNA fragments to obtain their mass spectra. Furthermore, the output prediction part 32, the output analysis part 35, and the data analysis part 33 of the control system simultaneously perform the analysis on SNPs of the predetermined number (n) of the different genome DNA fragments.

Page 46, please amend the paragraph beginning at line 18 as follows:

wherein m represents a predetermined natural number; w(n) represents a factor that represents the level of influence of the sample measured at ~~nth~~ n-th before the measurement of the sample which is measured at ~~ith~~ i-th.

IN THE CLAIMS:

Please amend claims 1-15 and 19 as follows:

1. (twice amended) A DNA analysis ~~system~~ method for analyzing DNA polymorphism, comprising the steps of:

~~ionization means for~~ generating plural kinds of multiply-charged ions of a test DNA fragment by ionization, where each of the multiply-charged ions has five or more charges;

~~mass spectrometric means for~~ performing a mass spectrometry on the multiply-charged ions formed by the ionization ~~means~~ so as to measure a mass spectrum of the test DNA fragment;

~~analyzing result prediction means that predicts~~ predicting possible mass spectrum patterns in each of two cases, where one of the two cases is that the test DNA fragment is polymorphic and an other of the two cases is that the test DNA fragment is not polymorphic, based on both an information ~~including a~~ about the number of each of four different nucleic acid bases that constitute the test DNA fragment and an information about a polymorphism point; and

~~comparative processing means for~~ comparing a plurality of the predicted mass spectrum patterns with the measured mass spectrum to determine a nucleic acid base on the polymorphism point.

2. (twice amended) The DNA analysis ~~system~~ method according to claim 1, wherein the ~~analyzing result prediction means predicts~~ step of predicting includes predicting a mass-to-charge ratio (m/z; m is an ion mass, z is a number of electric charges) of each of the plural kinds of multiply-charged ions in each of the two cases, and the ~~comparative processing means compares~~ step of comparing includes comparing the predicted mass-to-charge ratio (m/z) of the predicted mass spectrum patterns with a mass-to-charge ratio (m/z) of the measured mass spectrum.

3. (twice amended) The DNA analysis ~~system~~ method according to claim 1, wherein the ~~analyzing result prediction means predicts~~ step of predicting includes predicting a mass-to-charge ratio (m/z; m is an ion mass, z is the number of electric charges) of each of the plural kinds of multiply-charged ions and a relative ion intensity corresponding to the mass-to-charge ratio (m/z) in each of the two cases, and the ~~comparative processing means compares~~ step of comparing includes comparing the predicted mass-to-charge ratio (m/z) of the predicted mass spectrum patterns with a mass-to-charge ratio (m/z) of the measured mass spectrum and compares the predicted relative ion intensities of the predicted mass spectrum patterns with relative ion intensities of the measured mass spectrum.

4. (twice amended) The DNA analysis ~~system~~ method according to claim 1, further comprising the steps of:

sampling ~~means for~~ by supplying a sample including the test DNA fragment ~~to~~ for the ionization ~~means~~ intermittently at a predetermined time period; and

~~detecting output analysis means for~~ performing the following treatment to obtain S(i) for the measured mass spectrum (I(i)) at an ordinal number "i",

$$S(i) = I(i) - \sum_{n=1}^{m} w(n) I(i-n)$$

wherein m represents a predetermined natural number and w(n) represents a factor ~~that represents a level of influence~~ for the measured mass spectrum of the

sample measured at n-th before the measurement of the sample which is measured at i-th~~,~~; and

wherein the S(i) is compared with each of the predicted mass spectrum patterns.

5. (amended) The DNA analysis ~~system~~ method according to claim 1, wherein the ~~ionization means generates~~ step of generating multiply-charged ions of the test DNA fragment by the ionization ~~means using~~ uses an air atomization.

6. (amended) The DNA analysis ~~system~~ method according to claim 1, wherein a nucleic acid base of a single nucleotide polymorphism point in the test DNA fragment is specified.

7. (amended) The DNA analysis ~~system~~ method according to claim 4, further comprising the step of:

~~display means for~~ displaying the occurrence of an emergency when a maximum ion intensity detected by the mass ~~spectrometric means~~ spectrometry is smaller than a predetermined threshold.

8. (twice amended) The DNA analysis ~~system~~ method according to claim 7, further comprising the steps of:

~~communication means for~~ generating information about the occurrence of the emergency .

9. (twice amended) The DNA analysis ~~system~~ method according to claim 4, wherein the step of sampling ~~means~~ introduces a standard sample ~~into~~ for the ionization ~~means~~ when a maximum ion intensity of the measured mass spectrum by the mass ~~spectrometric means~~ spectrometry is smaller than a predetermined threshold.

10. (twice amended) The DNA analysis ~~system~~ method according to claim 9, wherein when a maximum ion intensity of a mass spectrum of the standard sample detected by the mass ~~spectrometric means~~ spectrometry is equal to or higher than the predetermined threshold, the sample where the maximum ion intensity of the mass spectrum is detected as one smaller than the predetermined threshold is re-supplied to the ionization ~~means~~ by the sampling ~~means~~.

11. (twice amended) The DNA analysis ~~system~~ method according to claim 9, further comprising the steps of:

utilizing a plurality of measurement systems, where each of the measurement systems comprises the steps of sampling ~~means~~, ~~the~~ ionization ~~means~~, and ~~the~~ mass ~~spectrometric means~~ spectrometry,

wherein when a maximum ion intensity of a mass spectrum of the standard sample detected by mass ~~spectrometric means~~ spectrometry in one measurement system of the plurality of measurement systems is smaller than the predetermined threshold, the sample where a maximum ion intensity of a mass spectrum is detected as one smaller than the predetermined threshold at the one measurement system is transmitted ~~to~~ for sampling ~~means~~ of another measurement system except the one measurement system.

12. (twice amended) The DNA analysis ~~system~~ method according to claim 9, further comprising the steps of:

utilizing a plurality of measurement systems, where each of the measurement systems comprises the steps of sampling ~~means~~, ~~the~~ ionization ~~means~~, and ~~the~~ mass ~~spectrometric means~~ spectrometry,

wherein when a maximum ion intensity of a mass spectrum of the standard sample detected by mass ~~spectrometric means~~ spectrometry in one measurement system of the plurality of measurement systems is smaller than the predetermined

threshold, a sample intended to be measured by the one measurement system is sent ~~to~~ for sampling ~~means~~ of another measurement system except the one measurement system.

13. (amended) A DNA analysis ~~system~~ method for analyzing DNA polymorphism, comprising the steps of:

sampling ~~means for~~ by supplying a sample including a test DNA fragment ~~to an~~ for ionization ~~means~~ intermittently at a predetermined time period;

~~the ionization means~~ generating plural kinds of multiply-charged ions of the test DNA fragment by ionization, where each of the multiply-charged ions has five or more charges;

~~mass spectrometric means~~ for performing a mass spectrometry on the multiply-charged ions formed by the ionization ~~means~~ so as to measure a mass spectrum of the test DNA fragment;

~~detecting output analysis means for~~ performing the following treatment to obtain S(i) for the measured mass spectrum (I(i)) at an ordinal number "i",

$$S(i) = I(i) - \sum_{n=1}^{m} w(n) I(i-n)$$

wherein m represents a predetermined natural number and w(n) represents a factor ~~that represents a level of influence~~ for the measured mass spectrum of the sample measured at n-th before the measurement of the sample which is measured at i-th;

~~analyzing result prediction means that predicts~~ predicting possible mass spectrum patterns in each of two cases, where one of the two cases is that the test DNA fragment is polymorphic and an other of the two cases is that the test DNA fragment is not polymorphic, based on both an information ~~including a~~ about the number of each of four different nucleic acid bases that constitute the test DNA fragment and an information about a polymorphism point, wherein the ~~analyzing result prediction means predicts~~step of predicting includes predicting a mass-to-charge ratio (m/z; m is an ion mass, z is a number of electric charges) of each of the

plural kinds of multiply-charged ions and a relative ion intensity corresponding to the mass-to-charge ratio (m/z) in each of the two cases; and

~~comparative processing means for~~ comparing a plurality of the predicted mass spectrum patterns with the measured mass spectrum to determine a nucleic acid base on the polymorphism point, wherein the ~~comparative processing means compares~~ step of comparing includes comparing the predicted mass-to-charge ratio (m/z) of the predicted mass spectrum patterns with a mass-to-charge ratio (m/z) of the measured mass spectrum and compares the predicted relative ion intensities of the predicted mass spectrum patterns with relative ion intensities of the measured mass spectrum, and wherein the S(i) is compared with each of the predicted mass spectrum patterns.

14. (amended) A DNA analysis ~~system~~ method for analyzing DNA polymorphism, comprising the steps of:

sampling ~~means for~~ by supplying a sample including a test DNA fragment ~~to an~~ for ionization ~~means~~ intermittently at a predetermined time period;

~~the ionization means~~ generating plural kinds of multiply-charged ions of the test DNA fragment ionization, where each of the multiply-charged ions has five or more charges;

~~mass spectrometric means for~~ performing a mass spectrometry on the multiply-charged ions formed by the ionization ~~means~~ so as to measure a mass spectrum of the test DNA fragment;

~~detecting output analysis means for~~ performing the following treatment to obtain S(i) for the measured mass spectrum (I(i)) at an ordinal number "i",

$$S(i) = I(i) - \sum_{n=1}^{m} w(n) I(i-n)$$

wherein m represents a predetermined natural number and w(n) represents a factor ~~that represents a level of influence~~ for the measured mass spectrum of the sample measured at n-th before the measurement of the sample which is measured at i-th;

~~analyzing result prediction means that predicts~~ predicting possible mass spectrum patterns in each of two cases, where one of the two cases is that the test DNA fragment is polymorphic and an other of the two cases is that the test DNA fragment is not polymorphic, based on both an information ~~including a~~ about the number of each of four different nucleic acid bases that constitute the test DNA fragment and an information about a polymorphism point, wherein ~~the analyzing result prediction means predicts~~step of predicting includes predicting a mass-to-charge ratio (m/z; m is an ion mass, z is a number of electric charges) of each of the plural kinds of multiply-charged ions and a relative ion intensity corresponding to the mass-to-charge ratio (m/z) in each of the two cases; and

~~comparative processing means for~~ comparing including calculating a total ion intensity of each of the predicted mass spectrum patterns with respect to a plurality of peaks in the range of a predetermined mass-to-charge ratio (m/z) and for selecting the predicted mass spectrum pattern which has a highest total ion intensity and comparing the predicted mass spectrum patterns having the highest total ion intensity with the measured mass spectrum to determine a nucleic acid base on the polymorphism point, and wherein the S(i) is compared with the selected predicted mass spectrum patterns.

15. (amended) A DNA analysis ~~system~~ method for analyzing DNA polymorphism, comprising:

sampling ~~means for~~ by supplying a sample including a test DNA fragment ~~to the~~ for ionization ~~means~~ intermittently at a predetermined time period;

~~the ionization means~~ generating plural kinds of multiply-charged ions of the test DNA fragment by ionization, where each of the multiply-charged ions has five or more charges;

~~mass spectrometric means for~~ performing a mass spectrometry on the multiply-charged ions formed by the ionization ~~means~~ so as to measure a mass spectrum of the test DNA fragment;

~~detecting output analysis means for~~ performing the following treatment to obtain S(i) for the measured mass spectrum (I(i)) at an ordinal number "i",

$$S(i) = I(i) - \sum_{n=1}^{m} w(n) I(i-n)$$

wherein m represents a predetermined natural number and w(n) represents a factor ~~that represents a level of influence~~ for the measured mass spectrum of the sample measured at n-th before the measurement of the sample which is measured at i-th;

~~analyzing result prediction means that predicts~~ predicting possible mass spectrum patterns in each of two cases, where one of ~~th3e~~ the two cases is that the test DNA fragment is polymorphic and the other is that the test DNA fragment is not polymorphic, based on both an information ~~including a~~ about the number of each of four different nucleic acid bases that constitutes the test DNA fragment and an information about a polymorphism point, wherein the ~~analyzing result prediction means predicts~~step of predicting includes predicting a mass-to-charge ratio (m/z; m is an ion mass, z is a number of electric charges) of each of the plural kinds of multiply-charged ions and a relative ion intensity corresponding to the mass-to-charge ratio (m/z) in each of the two cases; and

~~comparative processing means for~~ comparing a plurality of the predicted mass spectrum patterns with the measured mass spectrum to determine a nucleic acid base on the polymorphism point, wherein the ~~comparative processing means selects~~ step of comparing includes selecting the predicted mass spectrum pattern such that a sum of a square root of a difference between a relative intensity of the measured mass spectrum having the S(i) and a relative intensity of the predicted mass spectrum pattern is smallest.

19. (amended) The DNA analysis method according claim 16, wherein the steps of generating, performing and selecting are subsequently repeated, the measured mass spectrum pattern (I(i)) at an ordinal number "i" is subjected to the

following treatment to obtain S(i), and then the S(i) is compared with each of the plurality of the predicted mass spectrum patterns,

$$S(i) = I(i) - \sum_{n=1}^{m} w(n)I(i-n)$$

wherein m represents a predetermined natural number and w(n) represents a factor ~~that represents a level of influence~~ for the measured mass spectrum of the sample measured at n-th before the measurement of the sample which is measured at i-th.